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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/711,896	11/15/2000	Tohru Kayano	KAYANO I	8185

7590 09/29/2004

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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 09/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/711,896	KAYANO ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-25* is/are pending in the application.

4a) Of the above claim(s) *10-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-9,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 November 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed on 07/20/04 has been entered.

Applicants' Amendment

2) Acknowledgment is made of Applicants' amendment filed 7/13/04 in response to the final rejection mailed 01/21/04. The finality of the previous Office action is proper, because it was necessitated by Applicants' extensive amendments particularly to claim 1 which placed new relative immunoreactivity limitations on the claimed antibody, this changing the scope of the claim(s). This matter however is now moot in view of Applicants' request for continued examination filed 07/20/04.

Status of Claims

3) Claims 1, 4, 24 and 25 have been amended via the amendment filed 07/12/04.

The withdrawn claim 14 has been amended, although not indicated as being 'currently amended'.

Claims 3 and 26 have been canceled via the amendment filed 07/12/04.

Claims 1, 4-9, 24 and 25 are pending and are under examination.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Withdrawn

6) The rejection of claims 1, 4-9, 24 and 25 made in paragraph 21 of the Office Action mailed 01/21/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

7) The rejection of claim 1 made in paragraph 22 of the Office Action mailed under 35

U.S.C. § 112, first paragraph, as containing new matter, is withdrawn in light of Applicants' amendments to the claim. A modified rejection is set forth below.

8) The rejection of claims 1, 4-6, 24 and 25 made in paragraph 12 of the Office Action mailed 06/27/03 and maintained in paragraph 19 of the Office Action mailed 01/21/04 under 35 U.S.C. § 102(b) as being anticipated by Akita *et al.* (*J. Biol. Chem.* 272: 26595-26603, October 1997), is withdrawn in light of Applicants' amendments to claim 1. A modified rejection to cover the amended claim(s) is set forth below.

9) The rejection of claims 1 and 9 made in paragraph 14 of the Office Action mailed 06/27/03 and maintained in paragraph 20 of the Office Action mailed 01/21/04 under 35 U.S.C. § 103(a) as being unpatentable over Akita *et al.* (*J. Biol. Chem.* 272: 26595-26603, October 1997), is withdrawn in light of Applicants' amendments to claim 1. A modified rejection to cover the amended claim(s) is set forth below.

Response to Applicants' Arguments on Akita *et al.*

10) Applicants contend that from Figure 6A of Akita *et al.*, the immunoreactive intensity of mAb 25-2G with prohIL-18 appears to be lower than that with mature hIL-18, or at worst is no more than the same as that with mature hIL-18. Applicants conclude that Akita's mAb 25-2G is clearly different from the claimed antibody of claim 1. Applicants acknowledge that the immunoreactive intensity of mAb 25-2G antibody with prohIL-18 is higher than that with mature hIL-18 because the band corresponding to prohIL-18 is denser than the band corresponding to prohIL-18. Without more, Applicants submit that density of the bands does not directly indicate the immunoreactive intensity. Applicants state that the mature hIL-18 in Figure 6B is from prohIL-18 under the action of partially purified recombinant hICE, and that since the formation reaction of mature hIL-18 from prohIL-18 is not complete, the amount of mature hIL formed is relatively small. Applicants allege that the apparent higher density of the band corresponding to prohIL-18 in Figure 6B is just appearance. Applicants submit that the immunoreactive intensities of mAb 25-2G antibody with mature hIL-18 and prohIL-18 should be evaluated from the density and width of the bands as shown in Figure 6A.

Applicants' arguments have been carefully considered, but are non-persuasive. First, it should be noted that Applicants are not claiming a specific monoclonal antibody produced by a specific hybridoma cell line, for example, mAb-proHuIL18#75, but a generic antibody with the

recited relative immunoreactivity. The claimed product is an isolated antibody specific to an interleukin 18 precursor having a higher immunoreactivity to interleukin 18 precursor than against any other substance, and Akita *et al.* taught such an antibody. Contrary to Applicants' assertion, one of skill in the art would readily make out from the intensity of the immunoreactivity bands in Figure 6B of Akita *et al.* that Akita's antibody binds to pro hIL-8 with greater intensity that it does to an other substance, such as, mature IL-18. It is important to note that the instant specification explicitly describes the term 'immunoreactivity' as meaning 'the intensity of an immunoreaction' (see line 24 on page 7 of the instant specification). Indeed Applicants acknowledge this fact in their statement that the density of the bands for mature IL-18 and pro hIL-18 shown in Figure 6 are 'almost the same', as opposed to 'the same'. Akita's Figure 6 does teach that the mAb 25-2G reacted with higher intensity with prohIL-18 (see the bottom Figure 6B panel, the middle column). Figure 6A panel was not referred to by the Office (see paragraph 20 of the Office Action mailed 01/21/04). Moreover, the Figure 6 legend describes that the conditions used were the same for the reactions of the preparations used both in Figures 6A and 6B. There is nothing in the reference of Akita *et al.* which indicates that the denser or wider immunoreactivity band with prohIL-18 as depicted in Figure 6B is just appearance, or that the formation of mature hIL-18 from prohIL-18 in incomplete. Indeed, the appearance is one of the parameters used in the art to determine the relative higher immunoreactivity of an antibody. The clearly visible, more intense immunoreactivity of the prior art antibody with prohIL-18 as depicted in the bottom B panel of Figure 6 qualifies as higher immunoreactivity against prohIL-18 compared with the immunoreactive intensity with mature hIL-18 (i.e., any other substance), absent evidence to the contrary. Since Akita has shown that the antibody could be used in immunoblotting to identify prohIL-18, one of skill in the art would have the motivation to produce an immunoassay kit using Akita's antibody for the purpose of identification of prohIL-18.

Rejection(s) Maintained

11) The rejection of claims 1, 4-8 and 24 made in paragraph 23 of the Office Action mailed 01/21/04 under 35 U.S.C. § 103(a) as being unpatentable over Yong *et al.* (*Immunological Journal* 15: 226-228, October 1999 - original and English translation) in view of Campbell AM (*In: Monoclonal Antibody Technology.* Elsevier Science Publishers, The Netherlands, Chapter 1,

pages 1-32, 1984), is maintained for reasons set forth therein and in the paragraph below.

12) The rejection of claims 9 and 25 made in paragraph 24 of the Office Action mailed 01/21/04 under 35 U.S.C. § 103(a) as being unpatentable over Yong *et al.* (*Immunological journal* 15: 226-228, October 1999 - original and English translation) as modified by Campbell AM (*In*: *Monoclonal Antibody Technology*. Elsevier Science Publishers, The Netherlands, Chapter 1, pages 1-32, 1984) as applied to claims 1 and 24 above, is maintained for reasons set forth therein and herebelow.

Applicants contend that Yong *et al.* do not provide any motivation to obtain an antibody of 'a purified recombinant human IL-8 precursor expressed in *E. coli*', neither does Campbell. Applicants submit that even if the proposed combination were obvious, such combination would not reach or lead to the claimed subject matter. Applicants state that it would require undue experimentation by one of ordinary skill in the art to obtain the desired antibody.

Applicants' arguments have been carefully considered, but are non-persuasive. Contrary to Applicants' assertion, the generation of a monoclonal antibody to an art-known product, such as, a purified recombinant human IL-8 precursor, does not require undue experimentation by one of ordinary skill in the art, since methods of producing monoclonal antibodies are well known and routinely practiced in the art. As set forth in paragraphs 23 and 24 of the Office Action mailed 01/21/04, Yong *et al.* taught a purified recombinant human interleukin-18 precursor expressed in *E. coli* via a recombinant plasmid, pQEIL 18p. Yong *et al.* identified a 36 amino acid-long amino terminal end of hIL-18 precursor protein to be an unusual leader sequence. This leader sequence of the prior art is structurally identical to the instantly recited SEQ ID NO: 1 (see entire document, especially pages 5, 6, 8, 10 and 11; and Figures 1 and 2). Yong *et al.* do not teach an isolated antibody specific to the human interleukin-18 precursor or SEQ ID NO: 1 wherein the antibody is at least ten times more immunoreactive with the human interleukin-18 precursor than with mature interleukin 18.

However, methods of producing antibodies to a specific polypeptide were well known in the art at the time of the invention. Furthermore, Campbell taught that it is customary now for any group working on a macromolecule to both clone the genes coding for it and make antibodies to it sometimes without a clear objective for their application. Campbell also taught

that protein macromolecules can be studied in the field of research using these antibodies (see page 29, last paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to generate and isolate a monoclonal or polyclonal antibody or a hybridoma cell line to Yong's purified interleukin 18 precursor or the unusual leader sequence of SEQ ID NO: 1 using art-known antibody production or hybridoma techniques to produce the isolated antibody or hybridoma of the instant invention, with a reasonable expectation of success. The resultant antibody produced using the specific interleukin 18 precursor or its leader sequence as the immunogen is expected to bind to the homologous interleukin 18 precursor or its leader sequence with higher (i.e., at least 10 times higher) immunoreactive intensity than to mature interleukin 18, which was not the immunogen used to raise the antibody. Given Campbell's teaching that antibodies to a protein are made in the art without a clear objective for their application, one of skill in the art would have been *motivated* to produce the instant invention for the expected benefit of producing an antibody to Yong's protein in order to study the protein or the unusual leader sequence for research purposes as taught by Campbell. The rejection stands.

With regard to the rejection of claims 9 and 25 under 35 U.S.C. § 103(a) as being unpatentable over Yong *et al.* as modified by Campbell AM, the teachings of Yong *et al.* as modified by Campbell do not teach an immunoassay kit comprising an antibody to interleukin 18 precursor as recited, or the antibody contained in a pharmaceutically acceptable carrier.

However, methods of assembling an immunoassay kit using an antibody product was well known and routinely practiced in the art, and would have been obvious to a skilled artisan at the time the invention was made to produce such an immunoassay kit for diagnostic purposes using the antibody of Yong *et al.* as modified by Campbell *et al.* One of skill in the art would have been motivated to produce the instant invention for the expected benefit of making readily available the prior art antibody, or for commercializing the prior art antibody for diagnostic use, since it is routine and conventional to use antibody reagents in immunoassay kits.

Similarly, adding a pharmaceutically acceptable carrier to an antibody is routine and very conventionally practiced in the art. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add an art-known pharmaceutical

carrier to the prior art antibody of Yong *et al.* as modified by Campbell *et al.* to produce the instant invention with a reasonable expectation of success, since it is quite conventional to have an antibody mixed with in a pharmaceutical carrier for diagnostic purposes. The rejection stands.

With regard to Applicants' remarks on Yong *et al.*, it should be noted that Applicant has provided no evidence within the instant specification to demonstrate that the claimed antibody differs in any unexpected or unobvious manner from that which one of ordinary skill in the art would have expected to obtain upon combining the teachings of the cited references. It should be noted that what would reasonably have been known and used by one of ordinary skill in the art need not be explicitly taught. See *In re Nilssen*, 851 F.2d 1401, 7 USPQ2d 1500 (Fed. Cir. 1988). The test of obviousness is not express suggestion of the claimed invention in any and all of the references, but rather what the references taken collectively would reasonably have suggested to those of ordinary skill in the art presumed to be familiar with them. *In re Keller*, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981). Obviousness does not require absolute predictability, (see *In re Lamberti*, 192 USPQ 278), but only a reasonable expectation of success (see *In re O'Farrell*, 7 USPQ 2d 1673, Fed. Cir. 1988).

Rejection(s) under 35 U.S.C. § 112, First Paragraph

13) Claim 1 and those that depend therefrom are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. Claim 1, as amended, is directed to an isolated antibody specific to an interleukin 18 precursor which has a higher immunoreactivity to said interleukin 18 precursor than to mature interleukin 18 by 'at least' 10 times ...'. Applicants point to line 6 of page 7 through line 1 of page 8 as providing descriptive support for limitation. However, a review of this part of the specification shows that there is no descriptive support for this limitation. The specification, as originally filed, especially at lines 6-8 of page 35 states as follows:

> Each antibody exhibited an immunoreactivity against human IL-18 only at **about** 10% to about 2:% or less of that against human IL-l8 precursor. [Emphasis added]

The scope of the term 'at least 10 times' is not the same as the scope of the term 'about 10 times'. The term 'at least 10' encompasses 100, 1000, 10,000 etc., for which there exists no descriptive support within the instant specification. Therefore, the new limitations in the instant claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are invited to point to specific line and page numbers of the specification, as originally filed, that provide descriptive support for the limitations identified above, or to remove the new matter from the claim(s).

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

14) Claims 1, 4-9, 24 and 25 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 1 is indefinite and confusing in the recitation: 'antibody specific to an interleukin 18 precursor ..... which has higher immunoreactivity to said interleukin 18 precursor than to mature interleukin 18 by at least 10 times, ... which has a higher immunoreactivity against interleukin 18 precursor than against any other substance', because the term 'any other substance' includes or does not exclude 'mature interleukin 18'. It is unclear how the immunoreactivity of the antibody to interleukin precursor 14, as recited in lines 2-4 of the claim, can be limited to at least 10 times higher, whereas at the later part of the same claim, the immunoreactivity can broaden to any degree of immunoreactivity.

(b) Claim 1 is vague and indefinite in the use of the limitation: 'higher immunoreactivity' (see line 5). The limitation 'higher' is a relative term which renders the claim indefinite. The term 'higher' is not specifically defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not reasonably be appraised of the scope of the invention.

(c) For clarity and proper antecedence, in line 2 of claims 4 and 5, it is suggested that Applicants replace the limitation 'the precursor' with --the interleukin 18 precursor--.

(d) Claim 1 lacks proper antecedence in the limitation 'interleukin 18 precursor' (see line 5). Since the earlier part of the claim already includes the limitation 'interleukin 18 precursor', for proper antecedence, it is suggested that Applicants replace the limitation in line 5 of the claim with --said interleukin 18 precursor--.

(e) Claims 4-9, 24 and 25, which depend directly or indirectly from claim 1, are also rejected as being indefinite because of the indefiniteness or vagueness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

15) Claims 1, 4-6, 24 and 25 are rejected under 35 U.S.C. § 102(b) as being anticipated by Akita *et al.* (*J. Biol. Chem.* 272: 26595-26603, October 1997 - already of record).

In claim 1, as amended, the limitation 'any other substance' does not exclude mature interleukin 18. The phrase in claim 1 'antibody ... which has higher immunoreactivity against interleukin 18 precursor than against than against any other substance' allows the claimed antibody to have any degree of higher immunoreactivity against interleukin 18 precursor than against 'any other substance' including mature interleukin. Since 'mature interleukin 18' is included in the limitation 'any other substance', any antibody that shows any degree of higher reactivity with interleukin 18 precursor anticipates the claimed antibody. The immunoreactivity of the antibody, as recited in the last three lines of claim 1, encompasses the antibody's immunoreactivity to mature IL-18 which can be less than ten times immunoreactivity.

It is noted that the instant specification explicitly describes the term 'immunoreactivity' as meaning 'the intensity of an immunoreaction'. See line 24 on page 7 of the instant specification.

Akita *et al.* disclosed monoclonal or polyclonal antibodies having binding affinity to prohIL-18 as tested by immunoblotting (see Figure 6 footnote; and page 26601; 'Reagents and Antibodies' on page 26595). The prior art antibody which is used in immunoblotting is expected to be contained in a buffer or saline (i.e., physiologically acceptable carrier) since immunoblotting requires the antibody to be contained in a physiologically acceptable carrier. Akita *et al.* identified the amino acid sequence of the prohIL-18 in Figure 2 as containing, MAAEPVEDNCINFVAMKFIDNTLYFAIEDDENLESD, which is identical in structure to the

instantly recited SEQ ID NO: 1. Akita's Figure 6B shows that the antibody reacted with higher intensity, i.e., higher immunoreactivity, with prohIL-18 (see the bottom Figure 6B panel, the middle column). Akita's Figure 6B along with Figure 6 legend is reproduced herebelow:

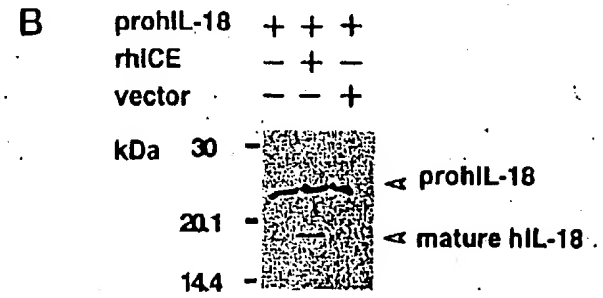

FIG. 6. *In vitro* cleavage assays for the identification of hIL-18-CE. *Panel A*, a preparation of prohIL-18 or prohIL-1β (about 100 ng each) were incubated at 37 °C for 3 h with partially purified hIL-18-CE (30 μl) in the presence of 20 mM Hepes, 10% glycerol, 2 mM DTT, at pH 7.4 in a total reaction volume of 50 μl. *I*, *Y*, and *N* denote iodoacetamide, Ac-YVAD-CHO, and without inhibitor, respectively. Cleaved products were analyzed by immunoblotting with anti-hIL-18 mAb (25-2G) or anti-hIL-1β pAb and visualized by enhanced chemiluminescence detection reagents. *Panel B*, a preparation containing about 100 ng of pro-hIL-18 was incubated with partially purified recombinant hICE (30 μl) with the same conditions as in *panel A*. *Vector* denotes the enzymatic preparation from COS-1 cells transfected with control vector (pCDM8). Cleaved products were visualized by immunoblotting as in Fig. 4A.

Clearly, Akita's antibody depicted in Figure 6B has higher immnoreactivity against interleukin 18 precursor than against mature interleukin 18 and therefor anticipates the instantly claimed antibody. Since the Patent Office does not have the facilities for examining and comparing Applicants' compound or product with that of the prior art, the burden is on Applicants to show that a difference exists between the claimed invention and that of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzerald et al.*, 05 USPQ 594.

Claims 1, 4-6, 24 and 25 are anticipated by Akita *et al.*

Rejection(s) under 35 U.S.C. § 103

16) Claim 9 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Akita *et al.* (*J. Biol. Chem.* 272: 26595-26603, October 1997) as applied to claim 1 above.

The teachings of Akita *et al.* are described above, which do not teach an immunoassay kit comprising an antibody to interleukin 18 precursor.

However, methods of assembling an immunoassay kit using an art-disclosed product was

well known and routinely practiced in the art, and would have been obvious to a skilled artisan at the time the invention was made to produce such a immunoassay kit for diagnostic purposes using the antibody of Akita *et al.* One of skill in the art would have been motivated to produce the instant invention for the expected benefit of making readily available Akita's antibody, or for commercializing Akita's antibody which are shown to have more intense immunoreactivity with interleukin 18 precursor than with mature interleukin 18, since it is routine and conventional to use an antibody reagent in immunoassay kits. Since Akita has shown that the antibody could be used in immunoblotting to identify prohIL-18, one of skill in the art would have the motivation to produce an immunoassay kit using Akita's antibody for the purpose of identification of prohIL-18.

Claim 9 is *prima facie* obvious over the prior art of record.

Remarks

17) Claims 1, 4-9, 24 and 26 stand rejected.

18) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of amendments, responses or papers is (703) 872-9306.

19) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

20) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be

reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

September, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER